



DHS SCIENCE AND TECHNOLOGY

Master Question List for COVID-19 (caused by SARS-CoV-2)

Weekly Report

18 March 2020

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FOREWORD

The Department of Homeland Security (DHS) is paying close attention to the evolving Coronavirus Infectious Disease (COVID-19) situation in order to protect our nation. DHS is working very closely with the Centers for Disease Control and Prevention (CDC), other federal agencies, and public health officials to implement public health control measures related to travelers and materials crossing our borders from the affected regions.

Based on the response to a similar product generated in 2014 in response to the Ebolavirus outbreak in West Africa, the DHS Science and Technology Directorate (DHS S&T) developed the following “master question list” that quickly summarizes what is known, what additional information is needed, and who may be working to address such fundamental questions as, “What is the infectious dose?” and “How long does the virus persist in the environment?” The Master Question List (MQL) is intended to quickly present the current state of available information to government decision makers in the operational response to COVID-19 and allow structured and scientifically guided discussions across the federal government without burdening them with the need to review scientific reports, and to prevent duplication of efforts by highlighting and coordinating research.

The information contained in the following table has been assembled and evaluated by experts from publicly available sources to include reports and articles found in scientific and technical journals, selected sources on the internet, and various media reports. It is intended to serve as a “quick reference” tool and should not be regarded as comprehensive source of information, nor as necessarily representing the official policies, either expressed or implied, of the DHS or the U.S. Government. DHS does not endorse any products or commercial services mentioned in this document. All sources of the information provided are cited so that individual users of this document may independently evaluate the source of that information and its suitability for any particular use. This document is a “living document” that will be updated as needed when new information becomes available.

SARS-CoV-2 (COVID-19)	Infectious dose – how much agent will make a normal individual ill?	Transmissibility – How does it spread from one host to another? How easily is it spread?	Host range – how many species does it infect? Can it transfer from species to species?	Incubation period – how long after infection do symptoms appear? Are people infectious during this time?
<p>What do we know?</p>	<ul style="list-style-type: none"> The human infectious dose of SARS-CoV-2, which causes coronavirus disease 19 (COVID-19) is currently unknown via all exposure routes. Animal data are used as surrogates. Rhesus macaques are infected with SARS-CoV-2 via the ocular conjunctival and intratracheal route at a dose of 700,000 PFU (10^6 TCID₅₀).⁵¹ A total dose of 700,000 plaque-forming units (PFU) of SARS-CoV-2 infected cynomolgus macaques via a combination intranasal and intratracheal exposure (10^6 TCID₅₀ total dose).¹⁰⁹ Macaques did not exhibit clinical symptoms, but shed virus through the nose and throat.¹⁰⁹ Nonhuman primate infection may not represent human infection. Initial experiments suggest that SARS-CoV-2 can infect genetically modified mice containing the human ACE2 cell entry receptor. Infection via the intranasal route (dose: 10^5 TCID₅₀, approximately 70,000 PFU) causes light infection, however no virus was isolated from infected animals, and polymerase chain reaction (PCR) primers used in the study do not align well with SARS-CoV-2, casting doubt on this study.¹⁴ The infectious dose for SARS in mice is estimated to be between 67-540 PFU (average 240 PFU, intranasal route).⁴⁹⁻⁵⁰ Genetically modified mice exposed intranasally to doses of MERS virus between 100 and 500,000 PFU show signs of infection. Infection with higher doses result in severe syndromes.^{7, 41, 81, 150} 	<ul style="list-style-type: none"> Pandemic COVID-19 has caused 214,894 infections and 8,732 deaths⁷² in at least 173 countries and territories (as of 3/18/2020).^{27, 114, 135} There are 7,769 SARS-CoV-2 cases across 50 US states, with 118 deaths. (as of 3/18/2020)⁷²; there is sustained community transmission of COVID-19 in the US.¹⁷ High-quality estimates of human transmissibility (R_0) range from 2.2 to 3.1.^{93, 98, 106, 142, 149} Early estimates of the attack rate in China range from 3%-10%, mainly in households.¹³⁷ SARS-CoV-2 is believed to spread through close contact and droplet transmission,³¹ with fomite transmission⁷³, i.e., germs left on surfaces, and close-contact aerosol transmission also plausible.²² SARS-CoV-2 replicates in the upper respiratory tract (e.g., throat), and infectious virus is detectable in throat and lung tissue for at least 8 days.¹³⁸ Pre-symptomatic¹⁵¹ or asymptomatic¹² patients can transmit SARS-CoV-2; between 12%⁵⁴ and 23%⁹⁰ of infections may be caused by asymptomatic or pre-symptomatic transmission. SARS-CoV-2 is present in infected patient saliva,¹²⁴ lower respiratory sputum,¹³¹ and feces.⁸⁶ Social distancing and behavioral changes are estimated to have reduced COVID-19 spread by 44% in Hong Kong,⁴⁷ and a combination of non-pharmaceutical interventions (e.g., school closures, isolation) are likely required to limit transmission.⁵⁹ Up to 86% of early COVID-19 cases in China were undiagnosed, and these infections were the source for 79% of documented cases.⁸⁴ 	<ul style="list-style-type: none"> Early genomic analysis indicates similarity to SARS,¹⁵⁴ with a suggested bat origin.^{5, 42, 154} Analysis of SARS-CoV-2 genomes suggests that a non-bat intermediate species is responsible for the beginning of the outbreak.¹⁰⁸ The identity of the intermediate host remains unknown.^{85, 87-88} Positive samples from the South China Seafood Market strongly suggests a wildlife source,³³ though it is possible that the virus was circulating in humans before the disease was associated with the seafood market.^{18, 43, 144, 148} Experiments suggest that SARS-CoV-2 Spike (S) receptor-binding domain binds the human cell receptor (ACE2) stronger than SARS,¹⁴¹ potentially explaining its high transmissibility; the same work suggests that differences between SARS-CoV-2 and SARS-CoV Spike proteins may limit the therapeutic ability of SARS antibody treatments.¹⁴¹ Modeling between SARS-CoV-2 Spike and ACE2 proteins suggests that SARS-CoV-2 can bind and infect human, bat, civet, monkey and swine cells.¹²⁹ There is currently no experimental evidence that SARS-CoV-2 infects domestic animals or livestock, though it is expected that some animal species could be infected. 	<ul style="list-style-type: none"> The best current estimate of the COVID-19 incubation period is 5.1 days, with 99% of individuals exhibiting symptoms within 14 days of exposure.⁷⁹ Fewer than 2.5% of infected individuals show symptoms sooner than 2 days after exposure.⁷⁹ The reported range of incubation periods is wide, with high-end estimates of 24,⁶⁰ 11.3,¹¹ and 18 days.⁸³ Individuals can test positive for COVID-19 despite lacking clinical symptoms.^{12, 35, 60, 120, 151} Individuals can be infectious while asymptomatic,^{31, 110, 120, 151} and asymptomatic individuals can have similar amounts of virus in their nose and throat as symptomatic individuals.¹⁵⁵ Infectious period is unknown, but possibly up to 10-14 days^{5, 84, 114} On average, there are approximately 4⁵⁴ to 7.5⁸³ days between symptom onset in successive cases of a single transmission chain. Most individuals are admitted to the hospital within 8-14 days of symptom onset.¹⁵³ Patients are positive for COVID-19 via PCR for 8-37 days after symptom onset.¹⁵³ Individuals may test positive via PCR for 5-13 days after symptom recovery and hospital discharge.⁷⁷ The ability of these individuals to infect others is unknown. According to the WHO, there is no evidence of re-infection with SARS-CoV-2 after recovery.⁷⁸ Experimentally infected macaques were not capable of being reinfected after their primary infection resolved.¹³

SARS-CoV-2 (COVID-19)	Infectious dose – how much agent will make a normal individual ill?	Transmissibility – How does it spread from one host to another? How easily is it spread?	Host range – how many species does it infect? Can it transfer from species to species?	Incubation period – how long after infection do symptoms appear? Are people infectious during this time?
<p>What do we need to know?</p>	<ul style="list-style-type: none"> • Human infectious dose by aerosol route • Human infectious dose by surface contact (fomite) • Human infectious dose by fecal-oral route 	<ul style="list-style-type: none"> • Capability of SARS-CoV-2 to be transmitted by contact with fomites (doorknobs, surfaces, clothing, etc.) – see also Experimental Stability • Superspreading capacity needs to be refined • Updated person to person transmission rates (e.g., R₀) as control measures take effect • What is the underreporting rate?⁷¹ • Can individuals become re-infected with SARS-CoV-2? • What is the difference in transmissibility among countries? • Is the R₀ estimate higher in healthcare or long-term care facilities? 	<ul style="list-style-type: none"> • What is the intermediate host(s)? • What are the mutations in SARS-CoV-2 that allowed human infection and transmission? • What animals can SARS-CoV-2 infect (e.g., pet dogs, potential wildlife reservoirs)? 	<ul style="list-style-type: none"> • What is the average infectious period during which individuals can transmit the disease? • Are individuals infectious after hospital discharge and clinical recovery, or are positive PCR tests only detecting non-infectious virus? • Can individuals become re-infected after recovery? If so, how long after?
<p>Who is doing experiments/has capabilities in this area?</p>	<p><i>Capable of performing work</i></p> <ul style="list-style-type: none"> - DHS National Biodefense Analysis and Countermeasures Center (NBACC) 	<p><i>Performing work:</i></p> <ul style="list-style-type: none"> - Christian Althaus (Bern) - Neil Ferguson (MRC) - Gabriel Leung, Joseph Wu (University of Hong Kong) - Sara Del Valle (Los Alamos) - Maimuna Majumder (Boston Children’s Hospital) - Trevor Bedford (Fred Hutchinson Cancer Center) - Sang Woo Park (Princeton) 	<p><i>Capable of performing work:</i></p> <ul style="list-style-type: none"> - Vincent Munster (Rocky Mountain National Laboratory) - Matthew Frieman (University of Maryland Baltimore) - Ralph Baric (University of North Carolina) - Stanley Perlman (University of Iowa) - Susan Baker (Loyola University Chicago) - Mark Denison (Vanderbilt University) - Vineet Menachery (University of Texas Medical Branch) - Jason McLellan, Daniel Wrapp, Nianshuang Wang (University of Texas) - David O’Conner (U. Wisconsin, Madison) 	<p><i>Performing work:</i></p> <ul style="list-style-type: none"> - Chaolin Huang (Jin Yin-tan Hospital, Wuhan, China) - The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team

SARS-CoV-2 (COVID-19)	Clinical presentation – what are the signs and symptoms of an infected person?	Clinical diagnosis – are there tools to diagnose infected individuals? When during infection are they effective?	Medical treatment – are there effective treatments? Vaccines?	Environmental stability – how long does the agent live in the environment?
<p>What do we know?</p>	<ul style="list-style-type: none"> The majority of COVID-19 cases are mild (81%, N = 44,000 cases)¹²⁰ Initial COVID-19 symptoms include fever (87.9% overall, but only 43.8% present with fever initially⁶⁰), cough (67.7%⁶⁰), fatigue, shortness of breath, headache, reduction in lymphocyte count,^{32, 38, 68} Headache³⁷ and diarrhea are uncommon^{68, 82} Complications include acute respiratory distress (ARDS observed in 17-29% of hospitalized patients,^{40, 67} which leads to death in 4-15% of cases^{40, 68, 130}), pneumonia,⁹⁶ cardiac injury, secondary infection, kidney failure, arrhythmia, sepsis, and shock.^{60, 68, 130, 153} Approximately 15% of hospitalized patients were classified as severe,^{60, 120} and approximately 5% of patients were admitted to the ICU.^{60, 120} Most deaths are caused by respiratory failure or respiratory failure combined with myocardial (heart) damage.¹¹¹ The case fatality rate (CFR) depends on comorbidities; cardiovascular disease, hypertension, diabetes, and respiratory conditions all increase the CFR.^{120, 153} The CFR increases with age; individuals older than 60 are at higher risk of death,^{120, 153} and >60% of confirmed fatalities have been male.¹²⁰ Children of all ages are susceptible to COVID-19,⁵³ though generally present with milder symptoms.³⁹ Severe symptoms in children, however, are possible.⁸⁹ In the US, 34% of hospitalizations have been individuals less than 44 years old.⁴ Based on one patient, a productive immune response is generated and sustained for at least 7 days.¹²¹ 	<ul style="list-style-type: none"> PCR protocols and primers have been widely shared among international researchers^{26, 45, 83, 116, 132, 136} though PCR-based diagnostic assays do not differentiate between active and inactive virus. A combination of pharyngeal (throat) RT-PCR and chest tomography are the most effective diagnostic criteria (correctly diagnosing 91.9% of infections).¹⁰⁴ Single throat swabs alone detect 78.2% of true infections, while duplicate tests identify 86.2% of infections.¹⁰⁴ Nasal and pharyngeal swabs may be less effective as diagnostic specimens than sputum and bronchoalveolar lavage fluid.¹³¹ RT-PCR tests are able to identify asymptomatic cases; SARS-CoV-2 infection was identified in 2/114 individuals previously cleared by clinical assessment.⁶⁶ The FDA released an Emergency Use Authorization enabling laboratories to develop and use tests in-house for patient diagnosis.⁵⁸ Updated tests from the US CDC are available to states.^{26, 31} US CDC has expanded patient testing criteria to include symptomatic patients at clinician discretion.¹⁶ Several rapid or real-time test kits have been produced by universities and industry, including the Wuhan Institute of Virology,⁴⁸ BGI,¹⁹ and Cepheid.¹²⁸ The US CDC is developing serological tests to determine what proportion of the population has been exposed to SARS-CoV-2.⁷⁴ Machine learning tools are being developed to predict severe and fatal COVID-19 cases based on CT scans.¹¹⁷ 	<ul style="list-style-type: none"> Treatment for COVID-19 is primarily supportive care, including mechanical ventilation and antibiotics to prevent secondary infection as appropriate.⁶⁰ Preliminary reports from two clinical trials in China suggest that favipiravir improves lung function and reduces recovery time in COVID-19 patients.¹²⁶ Early results suggest that tocilizumab may be effective at treating severe COVID-19 cases.¹⁴⁵ Press reports of a small clinical trial suggest that chloroquine is effective at reducing symptom duration.¹ Combination lopinavir and ritonavir with standard care was no more effective than standard care alone.²⁴ Corticosteroids are commonly given to COVID-19 patients¹⁵³ at risk of ARDS,¹⁴⁶ but their use is not recommended by the US CDC.²⁹ Multiple entities are working to produce a SARS-CoV-2 vaccine,⁸ including NIH/NIAD,^{63, 80} Moderna Therapeutics and Gilead Sciences,^{2-3, 94} and Sanofi with HHS.²¹ Moderna has begun phase 1 clinical vaccine trials in humans in WA state.¹⁰⁷ Regeneron Pharmaceuticals has developed potential SARS-CoV-2 antibody therapies.⁹⁹ The development of a coronavirus fusion inhibitor in the lab suggests efficacy across multiple human coronaviruses.¹⁴³ Takeda Pharma (Japan) is working to create antibody treatments based on infected patient plasma.⁶² 	<p><i>SARS-CoV-2 Data</i></p> <ul style="list-style-type: none"> SARS-CoV-2 can persist on plastic and stainless steel surfaces for up to 3 days (at 21-23°C, 40% RH), with a half-life of 13-16 hours.¹²⁵ SARS-CoV-2 has an aerosol half-life of 2.7 hours (particles <5 µm, tested at 21-23°C and 65% RH).¹²⁵ <p><i>Surrogate Coronavirus data:</i></p> <ul style="list-style-type: none"> Studies suggest that other coronaviruses can survive on non-porous surfaces up to 9-10 days (MHV, SARS-CoV)^{25, 36}, and porous surfaces for up to 3-5 days (SARS-CoV)⁵⁶ in air conditioned environments (20-25°C, 40-50% RH) Coronavirus survival tends to be higher at lower temperatures and lower relative humidity (RH),^{25, 36, 102, 127} though infectious virus can persist on surfaces for several days in typical office or hospital conditions¹²⁷ SARS can persist with trace infectivity for up to 28 days at refrigerated temperatures (4°C) on surfaces.²⁵ Beta-coronaviruses (e.g., SARS-CoV) may be more stable than alpha-coronaviruses (HCoV-229E).¹⁰² No strong evidence for reduction in transmission with seasonal increase in temperature and humidity.⁹² One hour after aerosolization approximately 63% of airborne MERS virus remained viable in a simulated office environment (25°C, 75% RH)¹⁰⁰ The aerosol survival of related human coronavirus (229E) was relatively high, (half-life of ~67 hours at 20°C and 50% RH), indicating ~20% of infectious virus remained after 6 days.⁷⁰ Both higher and lower RH reduced HCoV-229E survival; lower temperatures improved survival.⁷⁰

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<p>What do we need to know?</p>	<ul style="list-style-type: none"> • How long does it take for infected individuals to recover outside of a healthcare setting? • Is the reduction in CFR through time an indication of better treatment, less overcrowding, or both? 	<ul style="list-style-type: none"> • False positive/negative rates for tests • Eclipse phase of infection (time between infection and detectable disease) in an individual 	<ul style="list-style-type: none"> • Is GS-5734 (remdesivir) effective in vivo (already used in clinical trials under Emergency Use Authorization)?¹¹⁵ • Is the GLS-5000 MERS vaccine¹⁴⁷ cross-reactive against SARS-CoV-2? • Efficacy of antibody treatments developed for SARS^{46, 119} and MERS³⁴ • What is the efficacy of various MERS and SARS Phase I/II vaccines and other therapeutics? • Are viral replicase inhibitors such as beta-D-N4-hydroxycytidine effective against SARS-CoV-2?¹⁵ 	<ul style="list-style-type: none"> • Stability of SARS-CoV-2 in aerosol, droplets, and other matrices (mucus/sputum, feces) • Particle size distribution (e.g., droplet, large droplet and true aerosol distribution) • Duration of SARS-CoV-2 infectivity via fomites and surface (contact hazard)? • Stability of SARS-CoV-2 on PPE (e.g., Tyvek, nitrile, etc.)
<p>Who is doing experiments/has capabilities in this area?</p>	<ul style="list-style-type: none"> - Jin Yin-tan Hospital, Wuhan, China - China-Japan Friendship Hospital, Beijing, China - Peking Union Medical College, Beijing, China - Capital Medical University, Beijing, China - Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China - Huazhong University of Science and Technology, Wuhan, China - The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China - Tsinghua University School of Medicine, Beijing, China - Zhongnan Hospital of Wuhan University, Wuhan, China - Peking University First Hospital, Beijing, China - Peking University People's Hospital, Beijing, China - Tsinghua University-Peking University Joint Center for Life Sciences, Beijing, China - The Fifth Medical Center of PLA General Hospital, Beijing, China 	<p><i>Performing work:</i></p> <ul style="list-style-type: none"> - CDC - Wuhan Institute of Virology - Public Health Agency of Canada - Doherty Institute of Australia - Cepheid - BGI - Fudan University 	<p><i>Performing work:</i></p> <ul style="list-style-type: none"> - Peter Doherty Institute for Infection and Immunity - Academy of Military Medical Sciences, Beijing, China - Tim Sheahan (University of North Carolina) - Takeda Pharma. (Japan) - Regeneron Pharmaceuticals - CureVac (Germany) <p><i>Capable of performing work:</i></p> <ul style="list-style-type: none"> - Ralph Baric (University of North Carolina) - Matthew Frieman (University of Maryland Baltimore) - Sanofi, with BARDA - Janssen Pharma and BARDA⁶⁴ <p><i>Funded work:</i></p> <p>CEPI (\$24 million to seven groups):</p> <p>NIAID/NIH:</p> <ul style="list-style-type: none"> - Moderna and Kaiser Permanente for mRNA vaccine Phase I trial.³ - University of Nebraska Medical Center Trial (multiple therapeutics including Gilead's Remdesivir).² 	<p><i>Capable of performing work:</i></p> <ul style="list-style-type: none"> - Mark Sobsey (University of North Carolina) - DHS National Biodefense Analysis and Countermeasures Center (NBACC) - Defence Science and Technology Laboratory (Dstl) - Public Health Agency of Canada - CDC - EPA - NIH

SARS-CoV-2 (COVID-19)	Decontamination – what are effective methods to kill the agent in the environment?	PPE – what PPE is effective, and who should be using it?	Forensics – natural vs intentional use? Tests to be used for attribution.	Genomics – how does the disease agent compare to previous strains?
<p>What do we know?</p>	<p><i>SARS-CoV-2</i></p> <ul style="list-style-type: none"> Twice-daily cleaning with sodium dichloroisocyanurate decontaminated surfaces in COVID-19 patient hospital rooms.⁹⁵ Alcohol-based hand rubs are effective at inactivating SARS-CoV-2 in liquid.⁷⁵ EPA has released a list of SARS-CoV-2 disinfectants, but solutions were not tested on live virus.⁶ <p><i>Other Coronaviruses</i></p> <ul style="list-style-type: none"> Chlorine-based¹³⁴ and ethanol-based⁴⁴ solutions recommended. Heat treatment at 56°C is sufficient to kill coronaviruses,^{102, 152} though effectiveness depends in part on amount of protein in contaminated media¹⁰² 70% ethanol, 50% isopropanol, sodium hypochlorite [bleach, 200 ppm], and UV radiation are effective at inactivating several coronaviruses (MHV and CCV)¹¹² Ethanol-based biocides are effective disinfectants against coronaviruses dried on surfaces, including ethanol containing gels similar to hand sanitizer.^{69, 139} Surface spray disinfectants such as Mikrobac, Dismozon, and Korsolex are effective at reducing infectivity of the closely related SARS-CoV after 30 minutes of contact.¹⁰¹ Coronaviruses may be resistant to thermal inactivation for up to 7 days when stabilized in stool.¹²²⁻¹²³ Additionally, coronaviruses are more stable in matrixes such as respiratory sputum.⁵⁵ Hydrogen peroxide vapor is expected to be effective at repeated decontamination of N95 respirators based on other pathogens.¹⁰⁵ 	<ul style="list-style-type: none"> PPE effectiveness for SARS-CoV-2 is currently unknown; SARS is used as a surrogate. Healthcare worker illnesses (over 1,000¹²⁰) demonstrates human-to-human transmission despite isolation, PPE, and infection control.¹¹³ US CDC does not recommend the use of facemasks for healthy people. Facemasks should be used by people showing symptoms to reduce the risk of others getting infected. The use of facemasks is crucial for health workers and people in close contact with infected patients (at home or in a health care facility).²⁸ “Healthcare personnel entering the room [of SARS-CoV-2 patients] should use standard precautions, contact precautions, airborne precautions, and use eye protection (e.g., goggles or a face shield)”³⁰ WHO indicates healthcare workers should wear clean, non-sterile, long-sleeve gowns as well as gloves.¹³³ Respirators (NIOSH-certified N95, EUFP2 or equivalent) are recommended for those dealing with possible aerosols¹³⁴ Additional protection, such as a Powered Air Purifying Respirator (PAPR) with a full hood, should be considered for high-risk procedures (i.e., intubation, ventilation)²³ SARS-CoV-2 transmission has occurred in hospitals inside¹³⁰ and outside of China,⁶¹ including the US.²⁰ Porous hospital materials, including paper and cotton cloth, maintain infectious SARS-CoV for a shorter time than non-porous material.⁷⁶ Despite extensive environmental contamination, air sampling in patient rooms did not detect SARS-CoV-2.⁹⁵ 	<ul style="list-style-type: none"> Genomic analysis places SARS-CoV-2 into the beta-coronavirus clade, with close relationship to bat viruses. The SARS-CoV-2 virus is distinct from SARS and MERS viruses.⁵² Genomic analysis suggest that SARS-CoV-2 is a natural variant, and is therefore unlikely to be human-derived or otherwise created by “recombination” with other circulating strains of coronavirus.^{9, 154} Some genomic evidence indicates a close relationship with pangolin coronaviruses¹⁴⁰; data suggests that pangolins may be a natural host for beta-coronaviruses⁸⁷⁻⁸⁸. Additional research is needed. Genomic data support at least two plausible origins of SARS-CoV-2: “(i) natural selection in a non-human animal host prior to zoonotic transfer, and (ii) natural selection in humans following zoonotic transfer.”⁹ Either scenario is consistent the observed genetic changes found in all known SARS-CoV-2 isolates. Additionally, “[...] SARS-CoV-2 is not derived from any previously used virus backbone,” reducing the likelihood of laboratory origination,⁹ and “[...] genomic evidence does not support the idea that SARS-CoV-2 is a laboratory construct, [though] it is currently impossible to prove or disprove the other theories of its origin.”⁹ 	<ul style="list-style-type: none"> There have been no documented cases of SARS-CoV-2 prior to December 2019 Preliminary genomic analyses, however, suggest that the first human cases of SARS-CoV-2 emerged between 10/19/2019 – 12/17/2019.^{10, 18, 103} The mutation rate of SARS-CoV-2 is estimated to be similar to other RNA viruses (e.g., SARS, Ebola, Zika), and is currently calculated to be 1.04x10⁻³ substitutions per site per year (N = 116 genomes).⁶⁵ Preliminary phylogenetic analysis identified a very close genetic similarity between SARS-CoV-2 and a Bat coronavirus (RaTG13) isolated from Yunnan Province, China; suggesting that SARS-CoV-2 originated from bats.⁹⁷ Pangolin coronaviruses are closely related to both SARS-CoV-2 and the closely related Bat coronavirus (RaTG13); phylogenetic analysis suggested that SARS-CoV-2 is of bat origin, but is closely related to pangolin coronavirus.⁸⁷⁻⁸⁸ The Spike protein of SARS-CoV-2, which mediates entry into host cells and is the major determinant of host range, is very similar to the Spike protein of SARS-CoV.⁹¹ The rest of the genome is more closely related to two separate bat⁹¹ and pangolin⁸⁸ coronavirus. Analysis of SARS-CoV-2 sequences from Singapore has identified a large nucleotide (382 bp) deletion in ORF-8 that may result in an attenuated (less virulent) phenotype.¹¹⁸

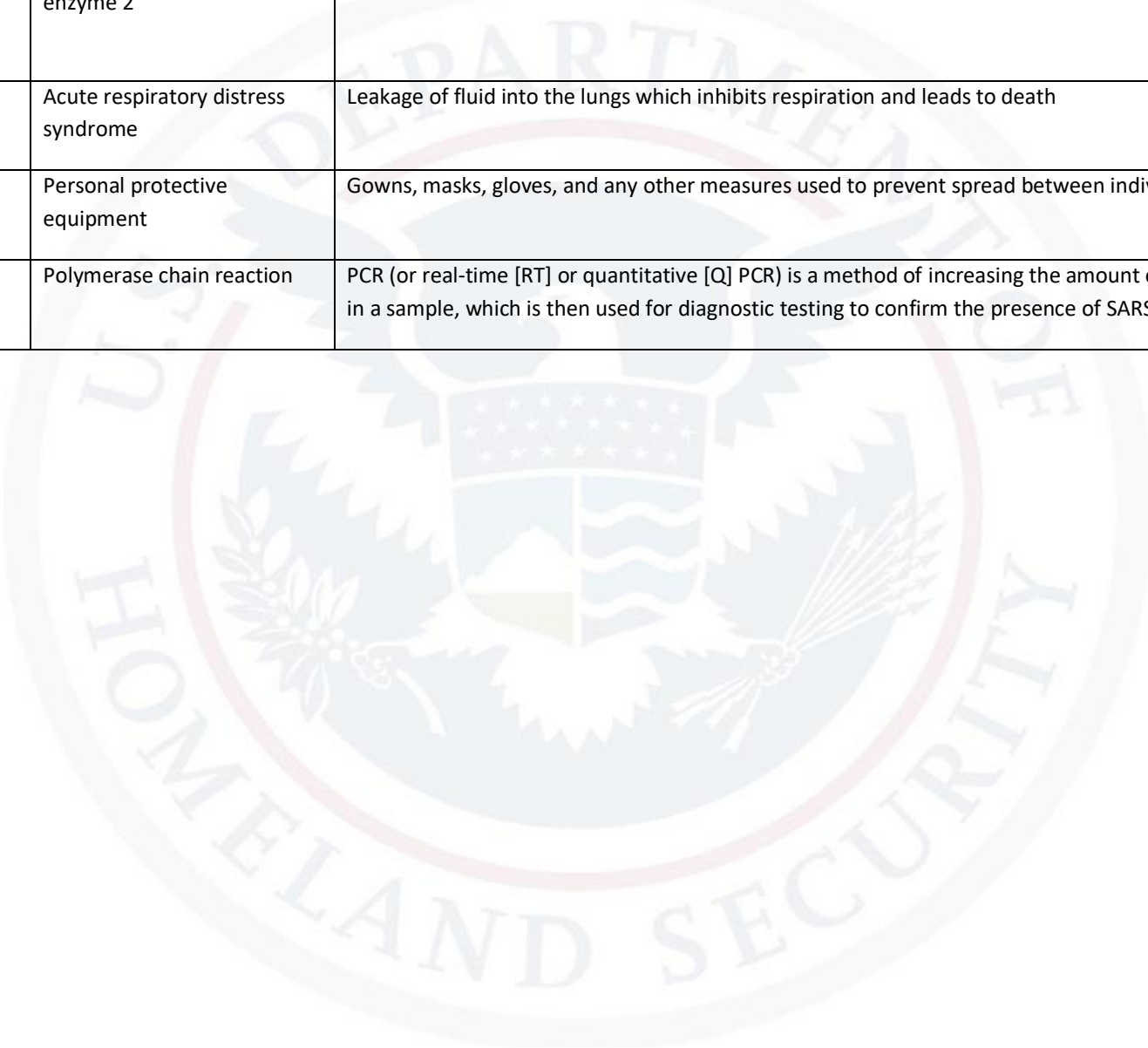
SARS-CoV-2 (COVID-19)	Decontamination – what are effective methods to kill the agent in the environment?	PPE – what PPE is effective, and who should be using it?	Forensics – natural vs intentional use? Tests to be used for attribution.	Genomics – how does the disease agent compare to previous strains?
<p>What do we need to know?</p>	<ul style="list-style-type: none"> • What is the minimal contact time for disinfectants? • Does contamination with human fluids/waste alter disinfectant efficacy profiles? • How effective is air filtration at reducing transmission in healthcare, airplanes and public spaces? 	<ul style="list-style-type: none"> • Mode of aerosol transmission? Effective distance of spread via droplet or aerosol? • How effective are barriers such as N95 respirators or surgical masks? • What is the appropriate PPE for first responders? Airport screeners? • Proper procedures for reducing spread in medical facilities / transmission rate in medical settings 	<ul style="list-style-type: none"> • What tests for attribution exist for coronavirus emergence? • What is the identity of the intermediate species? • Are there closely related circulating coronaviruses in bats or other animals with the novel PRRA cleavage site found in SARS-CoV-2? 	<ul style="list-style-type: none"> • Are there similar genomic differences in the progression of coronavirus strains from bat to intermediate species to human? • Are there different strains or clades of circulating virus? If so, do they differ in virulence?
<p>Who is doing experiments/has capabilities in this area?</p>	<p><i>Capable of performing work:</i></p> <ul style="list-style-type: none"> - DHS National Biodefense Analysis and Countermeasures Center (NBACC) 	<p><i>Generating recommendations:</i></p> <ul style="list-style-type: none"> - WHO - CDC - Pan-American Health Organization 	<p><i>Performing genomic investigations:</i></p> <ul style="list-style-type: none"> - Kristian Andersen, Andrew Rambaut, Ian Lipkin, Edward Holmes, Robert Garry (Scripps, University of Edinburgh, Columbia University, University of Sydney, Tulane, Zolgen Labs [Germantown, MD]) <p><i>Capable of performing work:</i></p> <ul style="list-style-type: none"> - Pacific Northwest National Laboratory - DHS National Biodefense Analysis and Countermeasures Center (NBACC) 	<p><i>Performing work:</i></p> <ul style="list-style-type: none"> - Trevor Bedford (Fred Hutchinson Cancer Research Center) - Ralph Baric, UNC - National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention - Shandong First Medical University and Shandong Academy of Medical Sciences - Hubei Provincial Center for Disease Control and Prevention - Chinese Academy of Sciences - BGI PathoGenesis Pharmaceutical Technology, Shenzhen, China - People's Liberation Army General Hospital, Wuhan, China - Wenzhou Medical University, Wenzhou, China - University of Sydney, Sydney, NSW, Australia - The First Affiliated Hospital of Shandong First Medical University (Shandong Provincial Qianfoshan Hospital), Jinan, China

Table 1. Definitions of commonly-used acronyms

Acronym/Term	Definition	Description
Attack Rate	Proportion of “at-risk” individuals who develop infection	Defined in terms of “at-risk” population such as schools or households, defines the proportion of individuals in those populations who become infected after contact with an infectious individual
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2	Official name for the virus previously known as 2019-nCoV.
COVID-19	Coronavirus disease 19	Official name for the disease caused by the SARS-CoV-2 virus.
CFR	Case Fatality Rate	Number of deaths divided by confirmed patients
PFU	Plaque forming unit	Measurement of the number of infectious virus particles as determined by plaque forming assay. A measurement of sample infectivity.
TCID ₅₀	50% Tissue Culture Infectious Dose	The number of infectious units which will infect 50% of tissue culture monolayers. A measurement of sample infectivity.
HCW	Healthcare worker	Doctors, nurses, technicians dealing with patients or samples
SARS	Severe Acute Respiratory Syndrome	Coronavirus with over 8,000 cases in global 2002-2003 outbreak
MERS	Middle-East Respiratory Syndrome	Coronavirus with over 2,000 cases in regional outbreak since 2012
CoV	Coronavirus	Virus typified by crown-like structures when viewed under electron microscope
R ₀	Basic reproduction number	A measure of transmissibility. Specifically, the average number of new infections caused by a typical infectious individual in a wholly susceptible population.
MHV	Mouse hepatitis virus	Coronavirus surrogate

CCV	Canine coronavirus	Canine coronavirus
Fomite	Inanimate vector of disease	Surfaces such as hospital beds, doorknobs, healthcare worker gowns, faucets, etc.
Droplet transmission	Sneezing, coughing	Transmission via droplets requires relatively close contact (e.g., within 6 feet)
Airborne transmission	Aerosolization of infectious particles	Aerosolized particles can spread for long distances (e.g., between hospital rooms via HVAC systems)
Transgenic	Genetically modified	In this case, animal models modified to be more susceptible to MERS and/or SARS by adding proteins or receptors necessary for infection
Intranasal	Agent deposited into external nares of subject	Simulates inhalation exposure by depositing liquid solution of pathogen/virus into the nose of a test animal, where it is then taken up by the respiratory system.
Incubation period	Time between infection and symptom onset	Time between infection and onset of symptoms typically establishes guidelines for isolating patients before transmission is possible
Infectious period	Length of time an individual can transmit infection to others	Reducing the infectious period is a key method of reducing overall transmission; hospitalization, isolation, and quarantine are all effective methods
Serial interval	Length of time between symptom onset of successive cases in a transmission chain	The serial interval can be used to estimate R_0 , and is useful for estimating the rate of outbreak spread
Superspreading	One individual responsible for an abnormally large number of secondary infections	Superspreading can be caused by high variance in the distribution of secondary cases caused by a single individual; most individuals infect very few people, while some infect a large number, even with the same average number of secondary infections
Nosocomial	Healthcare- or hospital-associated infections	Characteristic of SARS and MERS outbreaks, lead to refinement of infection control procedures

ACE2	Angiotensin-converting enzyme 2	Acts as a receptor for SARS-CoV, allowing entry into human cells
ARDS	Acute respiratory distress syndrome	Leakage of fluid into the lungs which inhibits respiration and leads to death
PPE	Personal protective equipment	Gowns, masks, gloves, and any other measures used to prevent spread between individuals
PCR	Polymerase chain reaction	PCR (or real-time [RT] or quantitative [Q] PCR) is a method of increasing the amount of genetic material in a sample, which is then used for diagnostic testing to confirm the presence of SARS-CoV-2



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